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10/520,685	05/27/2005	Allan Otto Fog Lihme	030307-0250	9774

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,685	LIHME ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed September 3, 2008 has been entered. Claims 2, 4-12, 15, 18-19, 24-25 and 27 have been amended. Claims 1, 3, 13-14 and 28 are canceled. Claims 2, 4-12, 15, 18-19, 24-25 and 27 are under consideration in this office action.

Withdrawal of Objections ad Rejections

2. The following objections and rejection are being withdrawn in view of applicants' amendments and arguments:

a) The objection of claim 2 drawn to the recitation of "….harmful substances responsible of inducing sepsis…" ;

b) The objection of dependant claims 3-12, 19, 24 and 28;

c) The objection of claims 3 and 17 under 37 CFR 1.75(c);

d) The rejection of claims 2, 4-5, 11-12, 15, 18, 24-28 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention; and

e) The rejection of claims 2-9, 11-12, 15-22 and 24-28 under 35 U.S.C. 102(a) as being anticipated by Lihme (WO 02/053251 published July 11, 2002).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2, 4-12, 15, 18-19, 24-25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The amended method's only active step comprises treating blood obtained from a mammal by passing blood through an adsorption column assembly. The is no recitation of an active step which removes harmful substances responsible for inducing sepsis caused by a gram negative or positive bacteria. There is no contact step to recite binding of the affinity specific molecules and the gram-negative or gram-positive bacteria. There is no correlation step which correlates treating blood by passing the blood through the column assembly and removing harmful substances responsible of inducing sepsis caused by gram-negative or gram-positive bacteria.

Response to Arguments

4. Applicant's arguments filed September 3, 2008 have been fully considered but they are not persuasive.

While applicants states that the amended address the rejection, it is the position of the Office that the claims still lack a complete recitation of the essential steps. As previous stated, the claims only method step is treating blood obtained from a mammal by passing blood through an adsorption column

assembly. Solely treating the blood will not achieve a removal of harmful substances responsible for inducing sepsis caused by gram negative or positive bacteria. The claims do not binding of the affinity specific molecules to the gram-negative or gram-positive bacteria, therefore it is unclear how the harmful substance can be retained within the column. Therefore the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 2, 4-8, 11-12, 15-21 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Zimmerman et al., (US Patent 6,090,292 published July 18, 2000).

The claims are drawn to an extracorporeal adsorption method for removing harmful substances responsible of inducing sepsis caused by Gram-negative bacteria in a mammal, wherein said method comprises treating blood obtained from said mammal by passing the blood through an adsorption column assembly at such a flow rate that a fluidized bed of the particles is formed and the harmful substances are removed from the blood by binding of the harmful substances to the affinity specific molecules, thereby retaining them in the

column, and wherein said adsorption column assembly comprises a column and an adsorption medium in the form of particles, the sedimented volume of said particles being at the most 80% of the volume of the column, said particles being characterized by carrying an affinity specific molecule with a specific affinity for the LPS portion of said Gram-negative bacteria, and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria.

Zimmerman et al., teaches an extracorporeal adsorption method for removing harmful substances caused by Gram-negative or Gram-positive bacteria in a mammal (col. 2, lines 25-28). Zimmerman et al., teach the method using an adsorption column assembly, comprising a column and an adsorption medium in the form of particles (col. 2, lines 43-48). Zimmerman et al., teach the sedimented volume of said particles being at the most 80% of the volume of the column (col. 3, lines 19-25). Zimmerman et al., teach the having particles carrying an affinity specific molecule with a specific affinity for Gram-negative bacteria wherein the method treats blood by passing the blood through the adsorption column assembly (col. 2, lines 28-30) at such a flow rate that a fluidized bed of the particles is formed (col. 3, lines 25-32).

Zimmerman et al., teach the adsorption column assembly is adapted for fluidized bed adsorption, in particular stabilized fluidized bed adsorption (col. 4, lines 45-65). Zimmerman et al., teach the particles have a density of at least 1.3 g/ml and a mean diameter in the range of 10-500 um (col. 2, lines 44-46). Zimmerman et al., teach the mammal being a human being (col. 2, lines 65-68). Zimmerman et al., teach the affinity specific molecule being a peptide, receptor

protein, multimeric arrangements or two or more different affinity specific molecules are present on particles within the adsorption medium (col. 3, lines 33-35 and col. 5, lines 35-43). Zimmerman et al., teach the flow rate of the blood through the column assembly is such that expansion ratio of the fluidized bed is at least 1.3 (col. 4, lines 65-68). Zimmerman et al., teach a method wherein a heparin substance is first injected into the blood stream of the mammal (col. 3-4, lines 66-3).

Thus, Zimmerman et al., teach the instantly claimed inventions.

Response to Arguments

6. Applicants' arguments filed September 3, 2008 have been fully considered but they are not persuasive. The rejection of claims 2, 4-8, 11-12, 15-21 and 24-27 under 35 U.S.C. 102(b) as being anticipated by Zimmerman et al., is maintained for reasons already of record.

Applicants' assert that Zimmerman *et al.* does not disclose the use of fluidized columns as in claims 2 and 27. However, Zimmerman et al., teach the adsorption column assembly is adapted for fluidized bed adsorption, in particular stabilized fluidized bed adsorption (col. 4, lines 45-65). Zimmerman et al., teach the method using an adsorption column assembly, comprising a column and an adsorption medium in the form of particles (col. 2, lines 43-48). Zimmerman et al., teach the sedimented volume of said particles being at the most 80% of the volume of the column (col. 3, lines 19-25). Zimmerman et al., teach the having particles carrying an affinity specific molecule with a specific affinity for Gram-

negative bacteria wherein the method treats blood by passing the blood through the adsorption column assembly (col. 2, lines 28-30) at such a flow rate that a fluidized bed of the particles is formed (col. 3, lines 25-32). Therefore, despite applicants' assertions, Zimmerman et al., clearly teaches the use of fluidized columns for extracorporeal adsorption methods.

Applicants' urge that Zimmerman *et al.,* does not teach how to construct a perfusable packing from 10-500 gm beads. However, the claims are not drawn to the construction of perfusable packing from 1-500 gm beads, therefore applicants' argument is not persuasive.

Applicants' state that the Zimmerman patent does not disclose the removal of bacteria or other bio-macromolecular entitles from blood only protein-bound toxins. However, Zimmerman et al., teaches an extracorporeal adsorption method for removing harmful substances caused by Gram-negative or Gram-positive bacteria in a mammal (col. 2, lines 25-28). Zimmerman et al., teach the having particles carrying an affinity specific molecule with a specific affinity for Gram-negative bacteria wherein the method treats blood by passing the blood through the adsorption column assembly (col. 2, lines 28-30). Zimmerman et al., teach the affinity specific molecule being a peptide, receptor protein, multimeric arrangements or two or more different affinity specific molecules are present on particles within the adsorption medium. Thus Zimmerman recites using the same type of affinity specific molecules as instantly recited by claims. Therefore assertions are not persuasive and the rejection of record is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 2, 4-7, 9-10, 16-18, 20-23 and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Jaber et al., (American Journal of Kidney Diseases. Vol. 30, No 5, Suppl. 4 (November), 1997: pages S44-S56).

The claims are drawn to an extracorporeal adsorption method for removing harmful substances responsible of inducing sepsis caused by Gram-negative bacteria in a mammal, wherein said method comprises treating blood obtained from said mammal by passing the blood through an adsorption column assembly at such a flow rate that a fluidized bed of the particles is formed and the harmful substances are removed from the blood by binding of the harmful substances to the affinity specific molecules, thereby retaining them in the column, and wherein said adsorption column assembly comprises a column and an adsorption medium in the form of particles, the sedimented volume of said particles being at the most 80% of the volume of the column, said particles being characterized by carrying an affinity specific molecule with a specific affinity for the LPS portion of said Gram-negative bacteria, and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria.

Jaber et al., teach extracorporeal adsorption method for treating gram-negative bacterial sepsis. Jaber et al., teach adsorbent-based blood purification founded upon adsorption, which removes harmful molecules by binding those molecules onto the surface of a material (page S44, col.2). Jaber et al., teach specific affinity molecules being antibodies coated onto micro spheres (page S53, col.1). See Table 1. Jaber et al., teach that polymyxinB has affinity for the Lipid A moiety of LPS from gram-negative bacteria (page S48, col. 2). Jaber et al., teach polymyxin B-Immobilized onto Sepharose bead with an affinity solid-phase column for the selective on-line removal of endotoxins during plasmapheresis (page S52, col. 1). Jaber et al., teaches using the affinity column device on rats in an on-line plasmapheresis with PMX-B sepharose beads having a diameter of 0.1 to 5um (page S52, col.1). Jaber et al., teach the endotoxin clearance rate was excellent (page S52, col.1). Jaber et al., also teach the use of polymyxin B-Immobilized macroporous cellulosic beads having a diameters of 60 to 80um, showing a more than 99.5% removal of endotoxins (page S52, col.1) Jaber et al., teach a flow rate of 200ml/min (page S53, col.1). Jaber et al., teach hemoperfusion methods wherein the flow rate was 80-100ml/min (page S50, col.2). Jaber et al., teach treating human whole blood or human plasma containing herapin or an anticoagulant on columns (page S49 col.2).

Therefore, Jaber et al., teach the instant claims.

Response to Arguments

8. Applicants' arguments filed September 3, 2008 have been fully considered but they are not persuasive. The rejection of claims 2, 4-7, 9-10, 16-18, 20-23 and 26-27 under 35 U.S.C. 102(b) as being anticipated by Jaber et al., is maintained for reasons already of record.

Applicants' assert that Jaber *et al.* does not disclose the use of fluidized columns as in claims 2 and 27. However, Jaber et al., teach adsorbent-based blood purification which removes bacterial molecules by binding those molecules onto the surface of a material. Jaber et al., teach beads with an affinity solid-phase column for the selective on-line removal of endotoxins wherein the beads have the instantly recited diameter and instantly claimed flow rate. Applicants assert that the antibody coated microsphere are different from the current invention. However, the particles of Jaber et al., meet the limitations of the claims, because the particles have the required density and fall within the range of the instantly recited mean diameter. Furthermore, the particles of jabber et al, and the instant application are all commercially available, therefore applicants' distinction is not persuasive.

Applicants' assert that Jaber et al., discloses the use of two extracorporeal circuits connected by a plasma filter being needed to circumvent direct contact between blood cells and microparticles, and a high-velocity centrifugal pump is necessary to keep the microparticles in suspension and circulation. However, the claim language recites the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended

and does not exclude additional, unrecited elements or method steps. See, e.g., *Mars Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended."). *Invitrogen Corp. v. Biocrest Mfg., L.P.,* 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."); *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986). Therefore applicants' arguments about additional elements disclosed by Jaber et al., are not persuasive, since Jaber et al., meets the limitations recited by the claims.

Applicants state that the system of Jaber *et al.* differs significantly from the present invention. It is noted that Applicants mere statements are not persuasive. Applicants argue that Jaber *et al.* does not teach or suggest a method for removing toxins from blood, based on the assembly of an adsorption column with such a flow rate that a fluidized bed of particles is formed, using molecules with a specific affinity for bacteria or bacteria-derived substances, see pending claim 2 and 27. Jaber et al., teach adsorbent-based blood purification that removes harmful molecules by binding those molecules onto the surface of a material using specific affinity molecules, such as antibodies or polymyxin-B

coated onto micro spheres because polymyxinB has affinity for the Lipid A moiety of LPS from gram-negative bacteria.

Finally applicants' argue that Jaber *et al.* does not suggest the use of a combination of molecules with a specific affinity along with the use of a fluidized bed. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., use of a combination of molecules with a specific affinity are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore applicants' argument is not persuasive and the rejection is maintained.

New Grounds of Objection Necessitated by Amendments

Claim Objections

9. Claims 2 and 4-12 are objected to because of the following informalities:

a) The last three lines of amended claim 2 recite "ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria, and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria." Therefore, appropriate correction is required.

b) Claim 2 delineates "ii" however there is previous delineation of "i." Therefore, appropriate correction is required.

New Grounds of Rejection Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2 and 4-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 recites the limitation "the affinity specific molecules" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

11. No claims allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory

action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645